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ORIGINAL ARTICLE

Gluten-Free Diet and Quality of Life in Patients with Screen-Detected Celiac Disease

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CONTEXT. Since the advent of serologic testing for celiac disease, most persons who receive a diagnosis of celiac disease have few or no symptoms. Although pathologic changes of celiac disease resolve on a gluten-free diet, how a gluten-free diet affects the quality of life for patients with screen-detected celiac disease is unclear.

OBJECTIVE. To evaluate the effect of a gluten-free diet on the quality of life of patients with screen-detected celiac disease.

DESIGN. Prospective study of patients before and 1 year after initiating a gluten-free diet.

PARTICIPANTS. 19 patients with screen-detected celiac disease (found by serologically testing first-degree relatives of celiac patients) and 21 consecutive patients with symptom-detected disease. In all cases, celiac diagnosis was confirmed by finding villous atrophy and crypt hyperplasia on small-bowel biopsy.

INTERVENTION. Gluten-free diet (explained during a single physician visit).

MAIN OUTCOME MEASURES. Gastrointestinal Symptoms Rating Scale (GSRS), in which scores range from 0 to 6 (higher scores represent worse symptoms); and quality of life measured with the Psychological General Well-Being Questionnaire (PGWB). Scores range from 22 to 132 (higher scores mean greater well-being).

RESULTS. At baseline, patients with symptom-detected celiac disease had poorer quality of life and more gastrointestinal symptoms than those with screen-detected celiac disease. Reported compliance with the gluten-free diet was good. All mucosal lesions of the small bowel had resolved at the follow-up biopsy. After 1 year of following the diet, quality of life for patients with screen-detected disease significantly improved (mean PGWB score increased from 108 to 114; P <0.01). A similar increase was noted in patients with symptom-detected disease (mean PGWB score increased from 92 to 103; P <0.01). Gastrointestinal symptoms also improved in patients with screen-detected disease and in patients with symptom-detected disease (mean GSRS scores decreased from 1.8 to 1.4 and from 2.6 to 1.9, respectively; P <0.01 for both comparisons).

CONCLUSIONS. Gluten-free diet was associated with improved quality of life for patients with symptom-detected celiac disease and patients with screen-detected celiac disease. Concerns about the burden of a gluten-free diet, at least over the short term, may be unfounded.

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Celiac disease is a genetic disorder characterized by small-bowel villous atrophy and crypt hyperplasia induced by daily ingestion of gluten from wheat, barley, and rye.[1,2] In Europe, the prevalence of celiac disease has been estimated to be 1 in 300 to 1 to 5000 persons,[3,4] but recent population-based screening studies suggest that the prevalence may be as high as 1 in 100[5–7] (and even higher in patients with autoimmune diseases[8]). In the United States, celiac disease remains rare—perhaps because the disease is underdiagnosed relative to Europe.[1,9] European physicians may be more familiar with celiac disease and may have a lower testing threshold. Most important, the use of serologic testing to screen for celiac disease is more common in Europe than in the United States.

In its classic form, celiac disease presents as a malabsorption syndrome, resulting in failure to thrive in children and weight loss and devastating diarrhea in adults. However, since the advent of serologic testing (by using a highly sensitive and specific immunoglobulin A endomysial assay), most cases of celiac disease have been diagnosed in persons with minimal or no symptoms—that is, in persons with clinically silent celiac disease.[10] Untreated celiac disease has been shown to predispose symptomatic patients to cancer (especially small-bowel lymphoma),[11–13] osteopenia,[14] miscarriages and infertility,[15,16] peripheral and central nervous system involvement,[17] and possibly autoimmune diseases.[18] Because these conditions may be the first signs of celiac disease,[19–26] some experts have called for population screening.

In symptomatic patients, a strict gluten-free diet is highly effective in alleviating symptoms[27] and may prevent long-term complications. The extent to which patients with screen-detected (i.e., symptomless) disease benefit from dietary restriction is unknown. Although some evidence suggests that such patients may have decreased bone mineral density that improves with a gluten-free diet,[28–30] a lifelong diet may be difficult to maintain.[31] Because persons with silent disease consider themselves healthy, receiving a diagnosis of silent celiac disease and adhering to a gluten-free diet may impair quality of life for these individuals. To help inform the debate on screening for silent celiac disease, we prospectively evaluated how the quality of life of patients with celiac disease detected on screening would change after diagnosis and 1 year of dietary treatment.

Methods

We prospectively studied gastrointestinal symptoms and quality of life in patients with screen-detected celiac disease and in patients with symptom-detected celiac disease before and 1 year after initiation of a gluten-free diet (**Figure 1**).

Patient Recruitment

Celiac Disease Patients

Nineteen patients with screen-detected celiac disease were identified by performing endomysial antibody testing on healthy first-degree relatives of patients with known celiac disease. Twenty-two consecutive patients with symptom-detected celiac disease served as a comparison group; one of these patients did not return the questionnaire and was excluded from the study.

Nonceliac Disease Participants

A second comparison group comprised 105 healthy participants without known celiac disease. To recruit this group, we asked 105 treated adult patients with celiac disease, who were selected from the member files of the Finnish Celiac Society, to give questionnaires to a person living in their neighborhood. This person could not have celiac disease nor have a family member with the disease and should eat a normal (i.e., a gluten-containing) diet. The 105 identified participants without celiac disease were not tested for endomysial antibodies, because given the prevalence of celiac disease in Finland (1 in 300 persons), this group probably included at most 1 person with undiagnosed celiac disease.

Study Protocol

Baseline Assessment

All study patients (participants with screen-detected disease and those with symptom-detected disease) received a diagnosis of celiac disease and treatment according to clinical protocol. During their first physician visit, the study patients underwent a physical examination and testing for endomysial antibodies; all patients found to have positive antibodies (serum dilution titers ranged from 1 in 5 to 1 in 8000) were referred for small-bowel biopsy. Together with the invitation for biopsy, participants received the self-administered baseline questionnaire by mail. To minimize physician influence on responses, questionnaires were self-administered and completed before the second physician visit. During the second visit, small-bowel biopsies were obtained. The findings of these biopsies (subtotal or severe partial villous atrophy and crypt hyperplasia) confirmed celiac disease in all cases.

The 105 participants in the nonceliac comparison group completed only the baseline questionnaire. (The Ethics Committee of Tempere University, which approved the study protocol, did not grant follow-up of these participants).

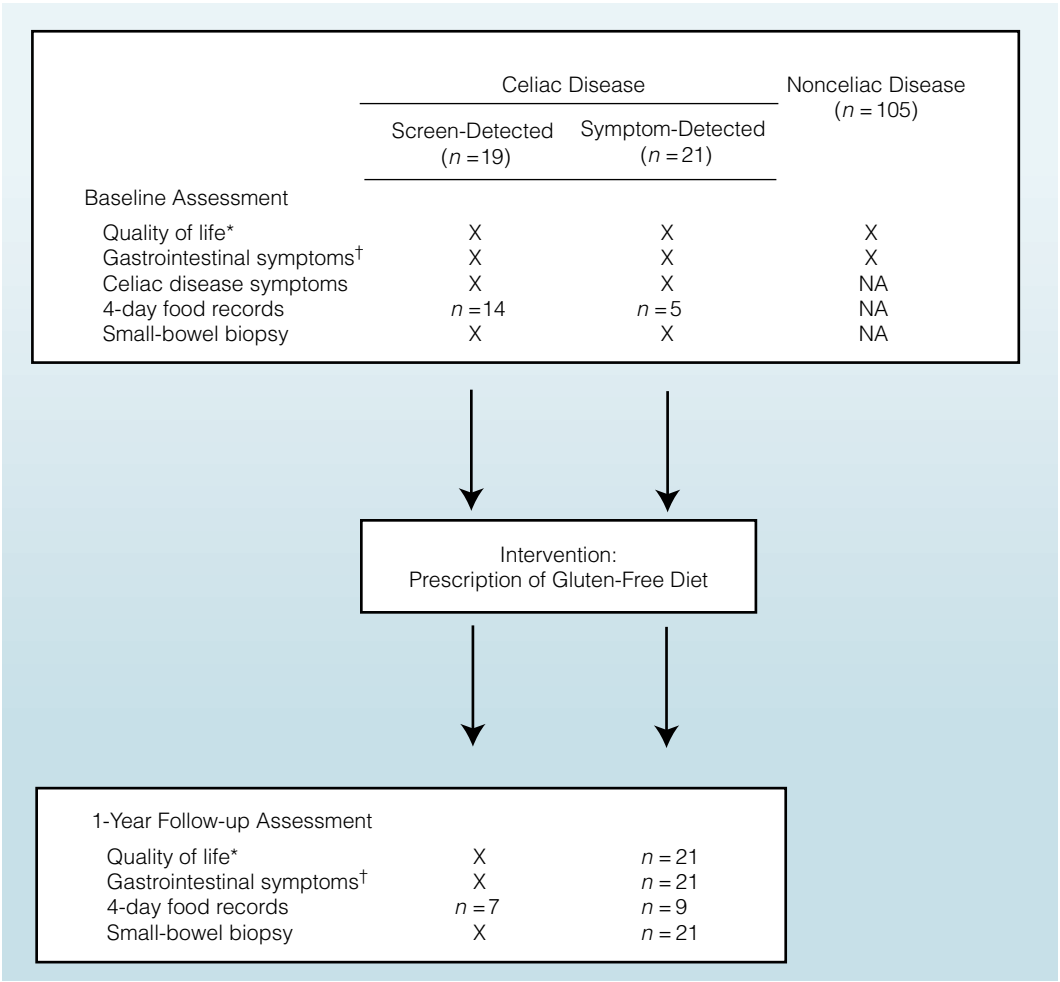

FIGURE 1. Study overview. *Assessed with the Psychological General Well-Being questionnaire. †Assessed with the Gastrointestinal Symptoms Rating Scale questionnaire.

Intervention

During the third visit, all patients with newly diagnosed celiac disease were informed about the disease and were counseled and prescribed a gluten-free diet (**Table 1**). We provided no other counseling or support during the following year.

Follow-up Assessment

One year after beginning the diet, all celiac patients underwent a second small-bowel biopsy and were asked to complete a follow-up questionnaire and a 4-day food record.

Measures

Quality of Life

We assessed general well-being using the Psychological General Well-Being (PGWB) scale—a 22-item questionnaire that includes both positive and negative affective states.[32] The questionnaire assesses six domains: anxiety, depressed mood, positive well-being, self-control, general health, and vitality. Question rating is based on a six-point Likert scale, with higher values indicating more satisfactory feelings. The total index is the sum of ratings on each question and ranges from 22 to 132 (with higher scores representing greater well-being). The PGWB is widely used and has proven reliability and validity.[33–35]

Gastrointestinal Symptoms

To assess gastrointestinal symptoms, we used the Gastrointestinal Symptoms Rating Scale (GSRS),[36] which consists of 15 items regarding five major gastrointestinal symptoms: diarrhea, indigestion, constipation, abdominal pain, and reflux. Question rating is based on a 6-point Likert scale, with lower values indicating fewer symptoms. The total index is the mean of these 15 items, varying from 0 to 6; a score of 0 indicates that no symptoms are present, and a score of 6 indicates the worst possible degree of all symptoms. The questionnaire has been used in many clinical trials[37–39] and has proven reliability.[40]

Other Characteristics

Patients were asked if they had any symptoms or signs suggestive of celiac disease, including tiredness, skin symptoms, infertility, osteoporosis, mouth symptoms, neurologic symptoms, iron deficiency anemia, or lactose

TABLE 1
Gluten-Free Dietary Treatment: Lifelong Avoidance of Gluten-Containing Products

Grains to avoid
Wheat
Barley
Rye
Permissable grains and flour products
Rice
Corn
Buckwheat
Millet
Oats
Industrially purified gluten-free flours
Sorghum
Flax
Soybean

intolerance. We also collected demographic information on age, sex, height, and weight (to calculate body mass index). Further, we asked the participants to assess their own current economic situation relative to the at-large population in Finland by having patients mark a visual analogue scale anchored at 0 (corresponding to the lowest possible status) and 100 (corresponding to the best possible economic situation in the society).

Dietary Adherence

At the outset, patients with celiac disease were asked to complete a 4-day food record to make sure that their current diet contained gluten. On the basis of these records, a dietitian estimated the mean gluten intake using the UNIDAP computer program (Unilever B.V., Rotterdam, Holland). The patients' self-concept of long-term adherence to the gluten-free diet was evaluated by using a visual analogue scale.[41,42] Patients indicated their level of adherence by marking a scale anchored at 0% and 100% compliant. At the end of the study, all patients were again asked to complete a 4-day food record.

Ethics

The Ethics Committee of Tampere University Hospital, Finland, approved the study protocol. Written informed consent was obtained from all participants. The hospital records and questionnaires were stored according to regulations of the European Community directives 269/92 and 270/92.

Statistical Analysis

We performed repeated measures analysis of covariance to study the significance of possible confounding factors (i.e., age, sex, economic situation, and body mass index) on general well-being or gastrointestinal symptoms. We found no evidence for confounding (i.e., crude and adjusted results were nearly identical). We report the adjusted results. Calculations were performed by using Statistica/Win software, 1998 edition (StatSoft Inc., Tulsa, OK).

Results

Patients with screen-detected celiac disease, patients with symptom-detected celiac disease, and the nonceliac disease participants were similar in age (late 40s). Approximately half the patients with screen-detected disease and most of the participants with symptom-detected disease as well as those without celiac disease were women (**Table 2**). Body mass index and economic situation did not differ significantly between the screen-detected and symptom-detected groups.

Celiac Disease Symptoms

Five of the 19 screen-detected patients reported signs or symptoms suggesting celiac disease. Three had received a diagnosis of lactose intolerance, 1 had iron deficiency anemia, and 2 had experienced vague arthralgias. We therefore performed separate analyses for the 14 asymptomatic patients. Among the 21 patients with symptom-detected disease, 16 presented with abdominal symptoms, 2 with stomatitis, 2 with iron-deficiency anemia, and 1 with neurologic symptoms.

Quality of Life

At baseline, the group without celiac disease and the group with screen-detected disease had similar scores for PGWB; these scores were significantly higher ($P < 0.01$) than those of the symptom-detected group (**Figure 2**). After 1 year of a gluten-free diet, mean PGWB scores increased from 108 (95% CI, 103 to 113) to 114 (CI, 110 to 118) in the screen-detected group and from 92 (CI, 85 to 99) to 103 (CI, 97 to 109) in the symptom-detected group. To put these scores in context, the mean PGWB score for patients with active reflux esophagitis was reported as 96,[43] duodenal ulcer had a score of 94,[43] and migraine had a score of 96.[33] The PGWB scores increased for 16 of the 21 patients in the symptom-detected group and for 18 of the 19 patients in the screen-detected group (the 1 patient with screen-detected disease whose quality of life worsened while adhering to a gluten-free diet had recently divorced). Follow-up PGWB scores for the symptom-detected group reached the level of the healthy comparison group. Follow-up scores for the screen-detected group exceeded the baseline scores of the nonceliac group.

In the screen-detected group, we found no statistically significant (or clinically important) difference between

TABLE 2

Demographic Data on Patients with Screen-Detected Celiac Disease, Patients with Symptom-Detected Celiac Disase, and Healthy Participants (Comparison Group)*

CHARACTERISTICS	SCREEN-DETECTED (*n* =19)	SYMPTOM-DETECTED (*n* =21)	NONCELIAC (*n* =105)
Median age (range), *yr*	48 (21–71)	49 (19–67)	48 (23–87)
Participants, *n*			
Women	10	17	90
Men	9	4	15
Median BMI, kg/m^2			
Women	25.5	23.3	—
Men	23.9	24.2	—
Economic situation†	58.4	57.0	—

**BMI = body mass index.*

†*Self-estimated economic situation measured by visual analogue scale with continuous scores ranging from 0 to 100.*

the PGWB values of the 14 asymptomatic patients and those of the 5 patients with mild symptoms (P =0.2).

Gastrointestinal Symptoms

The trend for gastrointestinal symptoms was analogous to those for well-being (**Figure 3**). Before commencement of the diet, gastrointestinal symptoms were significantly worse in the symptom-detected group than in the screen-detected group or nonceliac participants (P <0.01). Mean rating scores for gastrointestinal symptoms were similar in the screen-detected and nonceliac groups. For both groups with celiac disease, the major symptoms contributing to the total rating scores were indigestion and abdominal pain.

At follow-up, the mean total gastrointestinal score in the symptom-detected group decreased from 2.6 (CI, 2.2 to 3.0) to 1.9 (CI, 1.7 to 2.2), suggesting that their gastrointestinal symptoms were alleviated (achieving the level of the nonceliac group). The mean GSRS scores improved similarly for the screen-detected group (from 1.8 [CI, 1.5 to 2.1] to 1.4 [CI, 1.3 to 1.6]) and were even lower at the 1-year follow-up (i.e., better) than those of the nonceliac group at baseline. For context, patients with symptomatic celiac disease had GSRS scores in the same range as patients with severe esophageal reflux disease (mean total GSRS score, 2.9)[40] or duodenal ulcer (mean total GSRS score, 2.2).[43] Of note, in the screen-detected group, scores for the asymptomatic patients did not differ significantly from those of the patients with mild symptoms (P =0.06).

Gluten Intake and Dietary Adherence

Fourteen patients in the screen-detected group and 5 patients in the symptom-detected group agreed to complete a 4-day food record before starting a gluten-free diet. The records revealed that the gluten intake of these patients was similar to that of the normal population (average gluten consumption in patients with screen-detected and symptom-detected disease, respectively, were 3.2 g/d [range, 7.0 to 19.2 g/d] and 10.2 g/d [range, 4.7 to 14.7 g/d]).

After 1 year of a gluten-free diet, all patients described their mean long-term adherence to the gluten-free diet as intermediate or good. The mean self-estimated adherence on the visual analogue scale was 95% (range, 76% to 100%) in the screen-detected group and 93% (range, 60% to 100%) in the symptom-detected group. Furthermore, no dietary transgressions were observed in the 16 patients with celiac disease who agreed to complete the 4-day food record at follow-up. In support of the good reported dietary adherence, small-bowel biopsies repeated at 1 year demonstrated recovery of the mucosal lesion in all patients with screen- or symptom-detected disease.

Discussion

We examined the effect of a gluten-free diet on patients with clinically silent celiac disease—that is, among people who ingest gluten and feel healthy (or have only minor, nonspecific symptoms) despite having typical gluten-triggered lesions of the small-bowel mucosa.

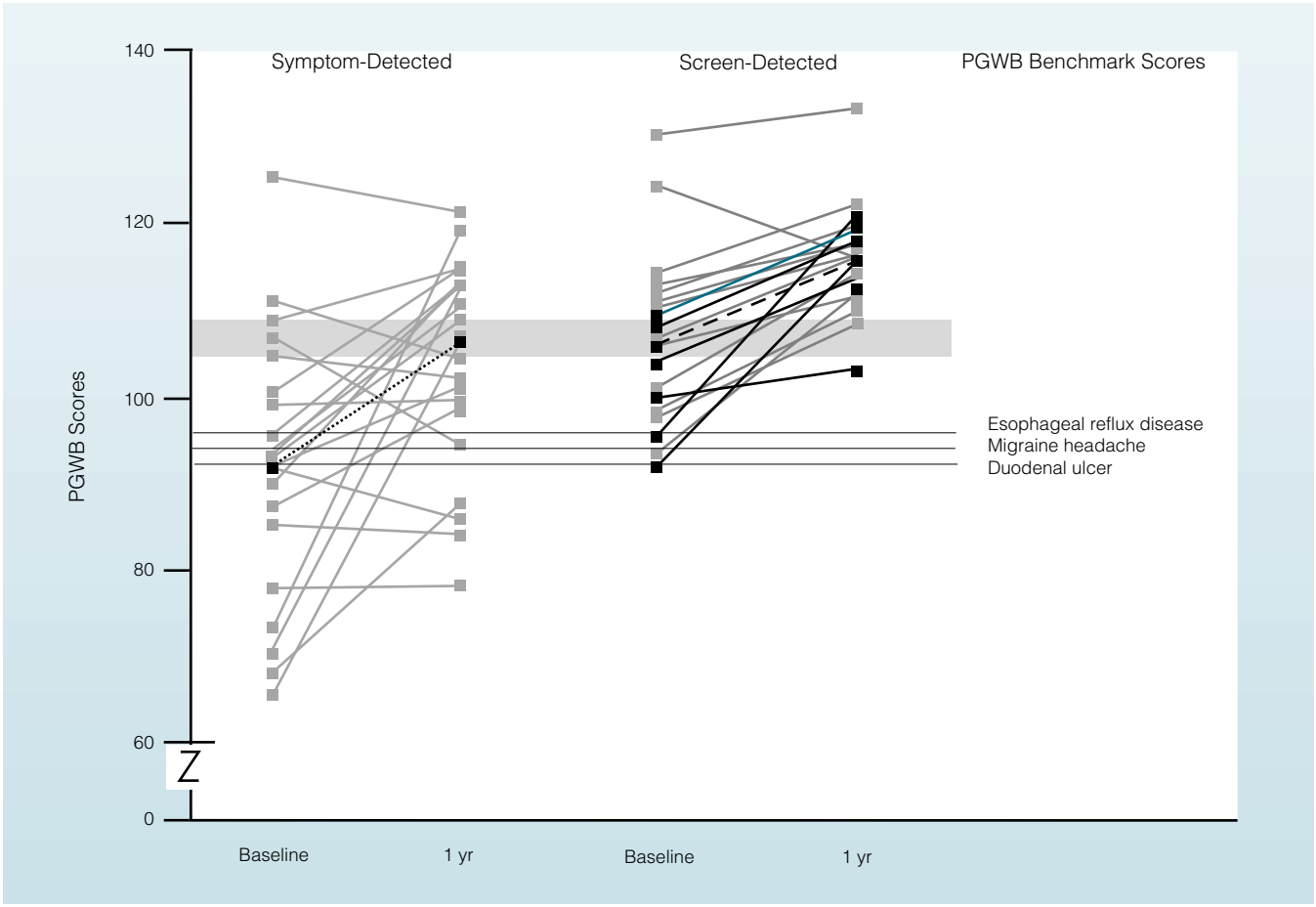

FIGURE 2. Psychological General Well-Being (PGWB) scores in patients with celiac disease before and 1 year after starting a gluten-free diet. The square dot line represents the change of mean total PGWB score in the symptom-detected group (n = 21). The dashed line corresponds to the change in mean total PGWB score in the group of screen-detected patients (n = 19). The solid black lines in the screen-detected group represent the 5 persons with mild symptoms. The blue line represents the change of mean total PGWB score of 14 asymptomatic patients (patients with mild symptoms were excluded from this analysis). The shaded horizontal area shows the 95% CIs for PGWB scores among a cross-sectional sample of 105 adults without celiac disease. Higher scores represent better quality of life.

Celiac disease in such individuals would remain undiagnosed without active serologic screening. In fact, it has been estimated that for every clinically diagnosed case of celiac disease as many as seven cases remain undiagnosed.[44] The value of diagnosing the disease in patients who feel healthy and prescribing a strict lifelong gluten-free diet in such patients is still unknown.

On the one hand, in some symptomless patients, the disease may manifest clinically later in life, even in elderly persons, with symptoms and signs of malabsorption.[2] The disease may also cause extra intestinal complications, even when gastrointestinal symptoms remain absent.[28–30, 45, 46] Early detection and treatment of celiac disease in these patients may prevent such complications. On the other hand, even with a gluten-containing diet, most persons with silent celiac disease might remain healthy throughout life without the burden of a gluten-free diet. In addition, asymptomatic persons may be harmed by being labeled as "patients" (i.e., they may start to behave as though they are sick after being told that they have a disease). Thus, an extremely important issue for these persons and for health care providers is whether we are doing more harm than good by diagnosing silent celiac disease through serologic screening tools and prescribing a gluten-free diet to persons with silent (symptomless) celiac disease.

We evaluated one important aspect of this issue—the influence of a gluten-free diet on the quality of life of patients with screen-detected celiac disease. Study participants were identified by actively screening healthy family members of persons with known celiac disease. Psychological general well-being and abdominal discomfort are highly subjective and personal matters that depend, at least in part, on personality and environment.[47] We used standardized, validated, and reliable questionnaires to assess these constructs, allowing us to compare patient groups with each other and with persons without celiac disease.[43] Reference values

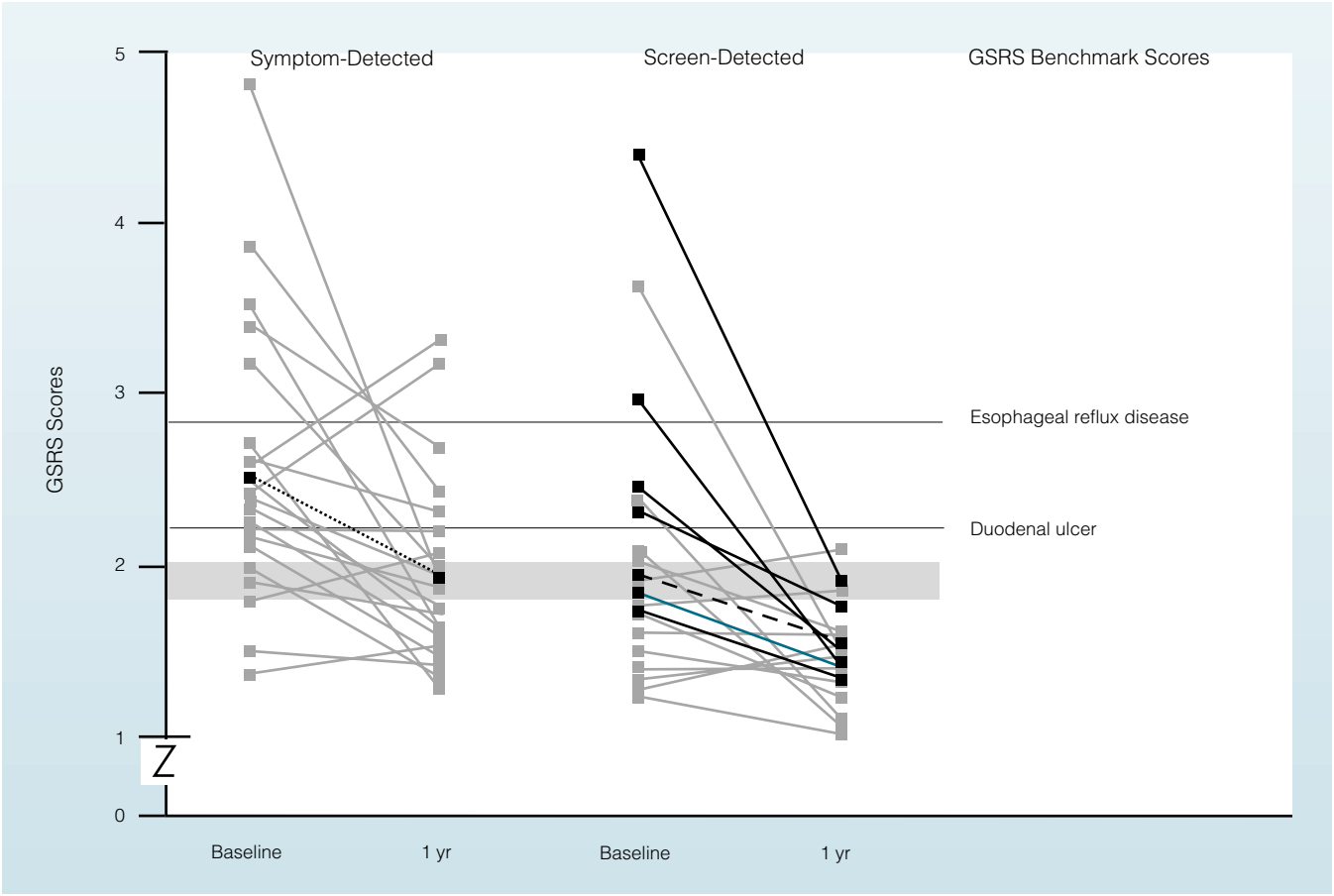

FIGURE 3. Gastrointestinal Symptoms Rating Scale (GSRS) scores in patients with celiac disease before and 1 year after starting a gluten-free diet. The square dot line represents the change of mean total GSRS score in the group (n = 21) of patients with symptom-detected celiac disease. The dashed line corresponds to the change in mean total GSRS score in the screen-detected group (n = 19). The solid black lines in the screen-detected group represent the 5 persons with mild symptoms. The blue line represents the change of mean total GSRS score of 14 totally asymptomatic patients (patients with mild symptoms were excluded from this analysis). The shaded horizontal area shows the 95% CIs for GSRS scores among a cross-sectional sample of 105 adults without celiac disease. Higher scores represent more severe gastrointestinal symptoms.

derived from a randomly selected Swedish sample of 4624 persons are available for both the PGWB and GSRS scores.[40] These values are similar to those we obtained in the group without celiac disease.

Our main finding is that after introduction of the gluten-free diet, most patients with symptom-detected disease and, interestingly, most patients with screen-detected celiac disease reported improved psychological well-being and gastrointestinal symptoms. During the diet, the well-being and gastrointestinal symptom scores of the screen-detected group (including both the truly asymptomatic and those with minor symptoms) improved, and their follow-up scores were actually better than those of the participants without celiac disease. These findings imply that before starting the diet, even the asymptomatic patients with celiac disease may have had mild symptoms, of which they became aware only after being prescribed a gluten-free diet. As expected, for patients with symptom-detected disease, psychological well-being and gastrointestinal symptoms improved during the diet, even more than for patients with screen-detected disease (achieving the level of the participants without celiac disease).

It should be emphasized that five patients in the screen-detected group who acknowledged minor symptoms consistent with celiac disease had the worst symptom and well-being scores in the screen-detected celiac group before the start of the diet; in this subgroup, quality of life improved most conspicuously during the diet. Without active screening, celiac disease in these patients might have remained undiagnosed or misdiagnosed for long periods. Quality of life for these persons did not diminish after diagnosis or while adhering to the restricted diet; in fact, it appeared to improve, providing some support for screening healthy persons, or at least those at high risk (e.g., close relatives of patients with known celiac disease).

Several study limitations should be acknowledged. First, although the quality of life of patients with screen-

or symptom-detected celiac disease improved during the first year of a gluten-free diet, we cannot determine whether such an effect is permanent. In fact, Hallert and colleagues[48] found that over a 10-year follow-up, patients with celiac disease failed to attain the same level of well-being as that of the general population. Moreover, Fabiani and associates[31] have suggested that long-term dietary adherence in patients with silent celiac disease is often poor. Thus, the improvement in quality of life that we have observed may only be temporary. In our study, the overall adherence among the patients with celiac disease was good. This may in part explain the improved quality of life observed during the first year of a gluten-free diet. In a previous study,[49] we found that long-term dietary adherence in patients with celiac disease was good and that quality of life was similar to that of the "normal" (i.e., persons without celiac disease) population. Patient encouragement and counseling may be crucial in attaining permanent improvement in quality of life. Unfortunately, our experience in Finland may not be generalizable to other countries—that is, adhering to a gluten-free diet may be more difficult for patients outside Finland, a country with an active celiac disease society. Finally, because we could not conduct follow-up assessments of well-being or symptoms in the healthy participants, our results should be interpreted with caution. It is possible, for example, that scores may improve simply as a result of sustained involvement in a study.

In conclusion, celiac disease represents a continuum that varies from absence of symptoms to severe malabsorption that can cause significant harm. Silent celiac disease is common, and the documented prevalence of the disease will increase with the advent of serologic screening. Our findings suggest that, at least over the short term, a gluten-free diet is acceptable and may even provide a quality-of-life benefit to patients with screen-detected celiac disease. Concerns about quality of life while adhering to a gluten-free diet may be unfounded. Nonetheless, more evidence about the long-term benefits (and harms) of early diagnosis and treatment of celiac disease is needed before starting population-based screening.

Take-Home Points

- **With the advent of serologic screening, diagnosis of symptomless celiac disease is becoming increasingly common.**
- **We evaluated the effect of a gluten-free diet on the quality of life of patients with screen-detected celiac disease using previously validated questionnaires to assess general well-being and gastrointestinal-specific symptoms.**
- **On average, after 1 year of a gluten-free diet, general well-being and gastrointestinal symptoms for patients with screen-detected celiac disease improved.**
- **It is not known whether a long-term gluten-free diet would remain acceptable to patients or if the diet prevents the complications associated with celiac disease.**

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